Contact Allergy to Preservatives

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Preservatives may be defined as chemicals added to topical drugs, cosmetics, toiletries, household products, and aqueous and emulsion systems in industry to prevent them from spoiling. They may act by interfering with certain chemical reactions or with the growth of molds, fungi, bacteria or parasites. The use concentration in the finished products is generally in the range of 0.01% to 1%. Owing to their inherent reactivity, many of these chemicals can induce allergic contact dermatitis (ACD). An overwhelming number of preservative formulations are marketed under various trade names and their synonyms. Unfortunately, there is no single source of information regarding the production, import and use of the different preservatives. The present paper focuses on four issues related to contact allergy to preservatives.

Relationship Between Predictive Test Results in Animals and Man and Clinical Experience

Chlorocresol is known to be a strong sensitizer in the guinea pig maximization test, with a frequency of positive reactions ranging from 15% to 84% of the animals tested, depending on the concentration used for induction. Interestingly, the use of chlorocresol as a preservative in topical corticosteroids is extensive, and in spite of that, clinical chlorocresol allergy occurs only sporadically [1].

Cytox 3522, containing 10% methylene-bis-thiocyanate, and equivalent products are used as biocides in industrial water systems. Cytox 3522 sensitized all animals in the guinea pig maximization test. In spite of that, human sensitization has not yet been reported. Exposed workers in a Finnish paper-manufacturing plant have been tested with a negative result [1]. The company uses about 25 tons per year of chemicals containing methylene-bis-thiocyanate. These two chemicals represent examples of strong experimental allergens used in the environment with a resulting low incidence of clinical contact allergy.

The parabens are moderate to weak experimental sensitizers. They are widely used and about 6000 of the 19,000 or so cosmetic formulas in the United States are preserved with parabens. Paraben allergy occurs with a frequency of around 1% in patch-test materials, which justifies the parabens being included in the standard series for patch testing. Among 8000 patients tested at Gentofte from 1971 to 1986,
0.8% of females and 1.2% of males were paraben-sensitive [16]. Earlier, when parabens were used in higher concentrations as antifungal agents, paraben sensitivity was more frequent.

Edman and Moller [8] and Gollhausen and co-workers [9] both found an increasing frequency of paraben sensitivity over the years among their eczema patients subjected to patch testing.


The predictive test data cannot stand alone but must be evaluated in relation to diagnostic patch tests and the exposure situation. There are examples of biocides with a strong allergenic potential in animal tests, but giving a low incidence of allergic contact dermatitis during practical use. There are biocides with a lower sensitizing potential which provoke a significant number of contact allergies, probably due to a widespread use often in higher concentrations.

We know from experimental and clinical data that allergic sensitization is dose-dependent. Therefore, it might be a good idea to also include dose-response determinations in standard predictive tests [1].

**Routine Patch Testing with Preservatives – Ingredient Labelling**

The Danish contact dermatitis research group tested a number of biocides on consecutive eczema patients in 1983–1984 [2]. Some positive reactions were found, but they were of limited clinical value because the results were frequently unexplainable. In most cases it was not possible to trace the exposure to the biocides in question. This is an argument for the demand on labelling of biocide content in all products, in order to make it easier to choose the appropriate biocides for testing of the patients.

**Kathon CG**

Kathon CG is of course very much in focus, due to its widespread use and the prevalence of contact allergy to it. De Groot and Weyland [11] have recently published a comprehensive review on Kathon CG. The literature contains pros and cons. The active ingredients in Kathon CG, methylchloroisothiazolinone and methylisothiazolinone are strong sensitizers in guinea pig allergy tests [4, 5]. A number of reports have documented a varying and in some countries an increasing incidence of allergic contact dermatitis to these chemicals [6, 11], which justifies the inclusion of Kathon CG in the standard series.